REMARKS

Claims 1-9 and 12-22 are currently pending. New claims 23-24 have been added. Support for new claims 23-24 can be found throughout the specification, including, for example, on pages 1-2, page 9, lines 18-21, page 11, line 20 to page 12, line 6, and page 18, line 28 to page 20, line 13. Applicants respectfully request reconsideration and allowance of all pending claims.

1. Rejection of the Claims under 35 U.S.C. §102(b) over O'Connor, et al.

Reconsideration is requested of the rejection of claims 1-9 and 12-22 under 35 U.S.C. §102(b) as being anticipated by O'Connor, et al. (U.S. Application Publication No. 2002/0045660).

Claim 1 is directed to a method of increasing lean body mass and reducing fat body mass in preterm infants. The method comprises feeding the preterm infant a nutritional formula comprising DHA and ARA from fish and fungal oil for the purpose of increasing lean body mass and reducing fat body mass in the preterm infant. The lean body mass of the preterm infant is increased by at least about 4% at 12 months corrected age as compared to preterm infants fed a control nutritional formula that does not comprise a source of DHA and ARA.

O'Connor, et al. is directed to "[m]ethods for providing nutrition and for enhancing neurological development of preterm

infants," and to "an improved nutritional composition containing specified amounts of [docosahexaenoic acid (DHA)] and [arachidonic acid (ARA)] as well as their precursor essential fatty acids alpha-linolenic and linoleic acids."[1] The method comprises feeding infants nutrient-enriched formulas supplemented with long chain polyunsaturated fatty acid, including both DHA and ARA, for an extended feeding regimen, typically at least three months corrected age, and preferably to 6 or 12 months corrected age.[2] O'Connor, et al. state that the methods described therein do not result in growth inhibition of the infants, such as that previously observed when DHA without ARA was used, and also result in improved or enhanced neurological development, such as visual, motor, and language development.[3]

Significantly, O'Connor, et al. fail to disclose or suggest feeding a nutritional formula comprising DHA and ARA to a preterm infant for the purpose of increasing lean body mass and reducing fat body mass in the infant, as required by claim 1. As noted above, O'Connor, et al. state that the ARA and DHA supplemented formulas described therein may improve or enhance neurological development, such as visual, motor, and language development, but do not disclose or suggest that such formulas have any effect on body composition, such as increasing lean body mass and reducing fat body mass.

[1] O'Connor, et al. at abstract.
[2] *Id.*
[3] *Id.* at paragraphs 64 and 66.

In the current action, the Office has once again taken the position that even though O'Connor, et al. do not literally disclose that a formula comprising DHA and ARA will increase lean muscle mass and reduce fat body mass in preterm infants, claiming a new use, new function, or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. Since the Office has persisted in maintaining this position, applicants assume the Office is either misinterpreting applicants' arguments regarding inherency or misinterpreting applicants' claims.

Specifically, it is respectfully submitted that whether or not the nutritional formulas of O'Connor, et al. inherently result in an increase in lean body mass and a reduction in fat body mass when fed to an infant **is irrelevant** to determining if O'Connor, et al. inherently discloses applicants' claimed method. As noted above, applicants' claim 1 specifically requires the nutritional formula comprising DHA and ARA be administered to the infant **for the purpose of** increasing lean body mass and reducing fat body mass in the infant. Thus, in order to anticipate applicants' claim 1, O'Connor, et al. must also disclose, either expressly or inherently, a method wherein a nutritional formula comprising DHA and ARA is administered to a preterm infant for the purpose of increasing lean body mass and reducing fat body mass in the infant. This is a limitation of applicants' claim 1 that cannot be ignored.

Applicants further note that there is no disclosure in O'Connor, et al. of administering a nutritional formula

comprising DHA and ARA to a preterm infant for the purpose of increasing lean body mass and reducing fat body mass in the infant. Nor has the Office pointed to anything in O'Connor, et al. to suggest that the methods of O'Connor, et al. inherently require feeding the formulas disclosed therein to a preterm infant for the purpose of increasing lean body mass and reducing fat body mass in the infant. At best, O'Connor, et al. disclose administering the ARA and DHA supplemented formulas described therein for the purpose of improving or enhancing neurological development, such as visual, motor, and language development, in an infant, but say nothing about their formulas having any effect on body composition, such as lean body mass and fat body mass, in the infant.

Applicants further note that a finding of inherency cannot be based on *mere assumptions* by the Office. Rather, to establish inherency, "the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art."[4] Furthermore, "[t]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic."[5]

[4] MPEP §2112 (citing *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original).

[5] MPEP §2112 (citing *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993)). MPEP §2112 also states "[i]nherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." (quoting *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999).

In the instant case, the Office has failed to provide any evidence or provide any basis for the position that O'Connor, et al. disclose feeding the formulas disclosed therein to a preterm infant for the purpose of increasing lean body mass and reducing fat body mass in the infant. What is relevant is that there is no disclosure, either expressly or inherently, in the O'Connor, et al. reference of feeding a nutritional formula comprising DHA and ARA to a preterm infant for the purpose of increasing lean body mass and reducing fat body mass in the infant. The mere fact that O'Connor, et al. disclose administering a nutritional composition comprising ARA and DHA to an infant does not mean O'Connor, et al. inherently (i.e., necessarily) disclose administering the composition for all purposes, or more specifically, for the purpose of increasing lean body mass and reducing fat body mass in the infant.

The Office has also stated that the neurological developments disclosed in O'Connor, et al. include motor development, and suggests that the lean body mass is mainly muscles and the motor development depends on muscle mass. Applicants respectfully disagree with the Office's interpretation of O'Connor, et al., and submit that this statement is not evidence that O'Connor, et al. inherently disclose applicants' claimed method.

Specifically, as noted above, the O'Connor, et al. method comprises feeding infants nutrient-enriched formulas supplemented with long chain polyunsaturated fatty acid, including both DHA and ARA, for an extended feeding regimen.

O'Connor, et al. state that the methods described therein do not result in growth inhibition of the infants, such as that previously observed when DHA without ARA was used, and also result in improved or enhanced neurological development, such as visual, motor, and language development. Applicants note, however, that the terms "growth" and "motor development," as used in O'Connor, et al., do not mean increasing lean body mass and reducing fat body mass.

For example, paragraph 109 of O'Connor, et al. clearly defines "growth" as "anthropometric growth," which generally refers to "the increase in physical size of the infant and is measured by physical metrics such as weight, length and head circumference." Nowhere do O'Connor, et al. indicate that "growth" has anything to do with increasing lean muscle mass and reducing fat body mass.

Likewise, paragraph 112 of O'Connor, et al. defines "motor development" as referring to "an infant's ability to control and coordinate its muscles to make desired movements—another measure of neurological development." O'Connor, et al. thus clearly indicate that "motor development" is a type of neurological development. Nowhere do O'Connor, et al. indicate that "motor development" has anything to do with increasing lean muscle mass and reducing fat body mass. Applicants further note that all infants have muscles, and presumably would be capable of showing an improvement in "motor development" if subjected to the O'Connor, et al. method. The Office, however, has failed to provide any evidence that an improvement in motor development is

in any way tied to an increase in lean muscle mass and a reduction in fat body mass.

As stated in MPEP §2131, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. Since O'Connor, et al. fail to disclose feeding a preterm infant a nutritional formula comprising DHA and ARA from fish and fungal oil for the purpose of increasing lean body mass and reducing fat body mass in the infant, and generally fail to disclose or suggest that the formulas disclosed therein have any affect on body mass, O'Connor, et al. fail to disclose each and every limitation of claim 1. As such, claim 1 is novel over the cited reference.

Claims 2-9 and 12-16 depend from claim 1 and are thus patentable over O'Connor, et al. for the same reasons as set forth above for claim 1, as well as for the additional elements they require.

Additionally, claim 16 depends from claim 1 and further comprises evaluating the lean body mass and fat body mass of the preterm infant after feeding the preterm infant the nutritional formula. The Office has stated that evaluating infant growth is done periodically as a routine and was done and disclosed by O'Connor, et al. However, as discussed above, "growth" as that term is used in O'Connor, et al. refers to "the increase in physical size of the infant," and was evaluated by O'Connor, et

al. by measuring weight, length and head circumference.[6] Nowhere do O'Connor, et al. disclose evaluating the lean body mass and fat body mass of an infant fed a nutritional formula comprising DHA and ARA. Claim 16 is thus patentable over O'Connor, et al. for this additional reason.

Claim 17 is directed to a method of increasing lean body mass and reducing fat body mass in preterm infants. The method comprises feeding the preterm infant a nutritional formula comprising DHA and ARA from fish and fungal oil; and evaluating the lean body mass and fat body mass of the preterm infant after feeding the preterm infant the nutritional formula. The lean body mass of the preterm infant is increased by at least about 4% at 12 months corrected age as compared to preterm infants fed a control nutritional formula that does not comprise a source of DHA and ARA. For the reasons set forth above for claim 16, applicants submit that O'Connor, et al. fail to disclose or suggest evaluating the lean body mass and fat body mass of an infant after feeding the infant the formulas disclosed therein. Claim 17 is thus also patentable over O'Connor, et al.

Claims 18-19 depend from claim 17 and are thus patentable over the cited reference for the same reasons as set forth above for claim 17, as well as for the additional elements they require.

[6] O'Connor, et al. at ¶ 109 and 175-176.

Independent claims 20 and 22 and new claim 23 are patentable over O'Connor, et al. for the same reasons as set forth above for claim 1.

Claim 21 depends from claim 20 and thus is patentable over the cited reference for the same reasons as set forth above for claim 20, as well as for the additional elements it requires.

New claim 24 is patentable over O'Connor, et al. for the same reasons as set forth above for claim 17.

2. Rejections of the Claims under 35 U.S.C. §102(b) over Koletzko

Reconsideration is requested of the rejection of claims 1 and 5 under 35 U.S.C. §102(b) as being anticipated by Koletzko ("Fatty acids and early human growth," Am. J. Clin. Nutr., 2001, Vol. 73:671-2).

Koletzko describes various studies evaluating the relationship between long-chain polyunsaturated fatty acids, and early human growth. Koletzko notes that there is a possible relationship between the supply and metabolism of different fatty acids and early human growth. Koletzko further states that the provision of infant formulas with a balanced supply of dietary arachidonic acid and docosahexaenoic acid in reasonable amounts and with adequate antioxidant protection, which is recommended by many experts worldwide, did not lead to poor growth or other adverse effects in several randomized clinical trials. Koletzko further notes that the quality of maternal

dietary fat consumption before and during pregnancy and lactation is of considerable importance for infants.[7]

Significantly, Koletzko fails to disclose or suggest feeding a preterm infant a nutritional formula comprising DHA and ARA from fish and fungal oil for the purpose of increasing lean body mass and reducing fat body mass in the preterm infant, as required by claim 1. Nor does Koletzko generally recognize or suggest that formulas comprising ARA and DHA increase lean body mass and reduce fat body mass. Rather, as noted above, Koletzko merely states that infant formulas with a balanced supply of dietary ARA and DHA did not lead to poor growth or other adverse effects in several randomized clinical studies.

The Office has stated that the long chain polyunsaturated fatty acids of Koletzko are of fish origin (citing to page 672) and the formula is given to infants who are born prematurely (citing to page 671). Applicants note, however, that the passage of Koletzko referred to by the Office as disclosing fish oil is actually describing a study which found that postnatal growth in premature infants was reduced by the feeding of formulas supplemented with fish oil "rich in the n-3 LCPUFA eicosapentaenoic acid but with no appreciable amount of AA."[8] There is no disclosure in Koletzko that the formulas used in this study contained DHA or ARA.[9] Furthermore, the passage of

[7] *See* Koletzko at p. 672.
[8] Koletzko at p. 672, bottom of first column (emphasis added).
[9] Applicants note that the two primary studies discussed in Koletzko (i.e., the Rump, et al. and Elias and Innis studies discussed on page 671 of Koletzko) both dealt with full term infants. Furthermore, Koletzko does not disclose the source of the DHA and/or ARA used in these studies, and it does

Koletzko referred to by the Office as disclosing administration of ARA and DHA to preterm infants is actually describing a completely separate study that recognized a correlation between the plasma lipid content of ARA and birth weight of infants born prematurely.[10] There is no disclosure in Koletzko that this study involved administration of formulas comprising ARA and DHA to preterm infants. There is thus no disclosure in Koletzko of feeding a preterm infant a nutritional formula comprising DHA and ARA from fish and fungal oil.

On page 5 of the current action, the Office has also asserted that O'Connor discloses the use of the same formula, and that recitation of the source of the long chain polyunsaturated fatty acids was disclosed in O'Connor, et al. Applicants respectfully submit that the disclosure of O'Connor, et al. is irrelevant in determining whether Koletzko anticipates claim 1. There is nothing in Koletzko to indicate that the infant formula referred to therein would be the same as the formulas disclosed in O'Connor, et al. and the Office has pointed to nothing to indicate that the Koletzko and O'Connor, et al. infant formulas would be the same.

The Office has also indicated that claiming a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.

---

not appear from the description in Koletzko that either of these studies involved administration of a nutritional formula comprising ARA and DHA to a preterm infant.

[10] *Id.* at p. 671, first paragraph.

As discussed above, whether or not a nutritional formula comprising DHA and ARA inherently results in an increase in lean body mass and a reduction in fat body mass when fed to a preterm infant **is irrelevant** to determining if Koletzko discloses applicants' claimed method. Claim 1 specifically requires a nutritional formula comprising DHA and ARA be administered to a preterm infant **for the purpose of** increasing lean body mass and reducing fat body mass in the infant. Thus, in order to anticipate applicants' claim 1, Koletzko must also disclose, either expressly or inherently, a method wherein a nutritional formula comprising DHA and ARA is administered to a preterm infant for the specific purpose of increasing lean body mass and reducing fat body mass in the infant. This is a limitation of applicants' claim 1 that cannot be ignored.

There is, however, clearly no disclosure or suggestion in Koletzko of administering a nutritional formula comprising DHA and ARA to a preterm infant for the purpose of increasing lean body mass and reducing fat body mass in the infant. At best Koletzko discloses that infant formulas with a balanced supply of dietary ARA and DHA in reasonable amounts and with adequate antioxidant protection, did not lead to poor growth or other adverse effects in several randomized clinical trials. There is nothing in Koletzko that suggests that ARA and DHA increase lean body mass and decrease fat body mass in infants.

Since Koletzko fails to disclose feeding a preterm infant a nutritional formula comprising DHA and ARA from fish and fungal oil for the purpose of increasing lean body mass and reducing

fat body mass in the infant, Koletzko fails to disclose each and every limitation of claim 1. As such, claim 1 is novel over the cited reference.

In the Response to Arguments section of the current action, the Office has stated that Koletzko teaches that there is an inverse relationship of total trans fatty acids to concentrations of various essential fatty acids in plasma lipids of mothers and infants. The Office concludes that since it is reported that the combination of ARA and DHA reduces plasma content of fat and consequently the fat that reaches the cells, and that it correlates to weight growth, then it is expected that the growth correlated with the administration of ARA and DHA is achieved in protein content of the cells, i.e., mainly muscular tissue. Applicants respectfully disagree.

Initially, applicants respectfully submit that the Office appears to be misinterpreting the Koletzko reference. Specifically, contrary to the Office's assertion, Koletzko does not state that administration of ARA and DHA in reasonable amounts is correlated to weight growth of infants. Rather, Koletzko merely states that infant formulas with a balanced supply of dietary ARA and DHA in reasonable amounts did not lead to poor growth or other adverse effects in several randomized clinical trials.[11]

Furthermore, nowhere does Koletzko disclose or suggest that the combination of ARA and DHA reduces plasma content of fat,

[11] *See* Koletzko at p. 672.

and consequently the fat that reaches cells. Rather, Koletzko merely describes a study in which the authors of the study report on an inverse relation of total *trans* fatty acids to concentrations of various essential fatty acids in plasma lipids of both mothers and infants. Koletzko states that these inverse correlations may reflect either potential inverse associations of dietary intakes of *trans* and essential fatty acids in the mothers, reflecting their food choices, or the metabolic suppression of essential fatty acid desaturation by *trans* isomers. Koletzko does not, however, state that the essential fatty acids referred to in the study are ARA and DHA, or that the inverse relation of total *trans* fatty acids to concentrations of various essential fatty acids in plasma lipids results in a reduction of plasma content of fat or the fat that reaches cells, or in the reduction of fat body mass. Additionally, Koletzko indicates that firm conclusions on cause and effect cannot be drawn from correlations found in these observational studies, because several confounding factors may have influenced the results.[12]

Applicants thus submit that the Office's assertion about Koletzko does not support a finding that Koletzko inherently discloses applicants' claimed method.

Claim 5 depends from claim 1 and is thus patentable over the cited reference for the same reasons as set forth above for claim 1 as well as for the additional elements it requires.

[12] *See id.*

New claim 23 is patentable over Koletzko for reasons similar to those set forth above for claim 1. Specifically, Koletzko fails to disclose feeding an infant a nutritional formula comprising a source of DHA and ARA for the purpose of increasing lean body mass and reducing fat body mass in the infant.

Additionally, with regard to new claim 24, applicants submit that Koletzko fails to disclose or suggest evaluating the lean body mass and fat body mass of an infant after feeding the infant a nutritional formula comprising DHA and ARA. Claim 24 is thus also patentable over Koletzko.

3. Rejections of the Claims under 35 U.S.C. §102(b) over Innis, et al.

Reconsideration is requested of the rejection of claims 1 and 5 under 35 U.S.C. §102(b) as being anticipated by Innis, et al. ("Docosahexaenoic acid and arachidonic acid enhance growth with no adverse effects in preterm infants fed formula," J. Pediat., May 2002, Vol. 140, No. 5, pp. 547-54).

Innis, et al. describe a study testing the effects of DHA and ARA supplementation on growth or visual acuity of formula-fed premature infants. Specifically, the Innis, et al. study gave premature infants preterm formula with either no DHA or ARA (control), 0.15% energy DHA, or 0.14% DHA plus 0.27% ARA from single-cell triglycerides for at least 28 days, and then fed the infants term formula (with no DHA or ARA) to 57 weeks postmenstrual age. The results of the Innis, et al. study found

that infants fed the DHA plus ARA formula gained weight significantly faster during preterm formula feeding than control infants, had weights and weight:length ratios not different from term breast-fed infants at 48 and 57 weeks PMA, and that providing DHA or DHA plus ARA during the preterm period had no effect on subsequent visual acuity or incidence of adverse events. Innis, et al. concluded that feeding DHA plus ARA from single-cell triglycerides enhances weight gain in formula-fed premature infants with no evidence of adverse effects.[13]

Significantly, Innis, et al. fail to disclose or suggest feeding a preterm infant a nutritional formula comprising DHA and ARA from fish and fungal oil for the purpose of increasing lean body mass and reducing fat body mass in the infant. Nor do Innis, et al. generally recognize or suggest that formulas comprising ARA and DHA increase lean body mass and reduce fat body mass. Rather, as noted above, Innis, et al. merely evaluated the effects of ARA and DHA supplemented formulas on the growth or visual acuity of formula-fed premature infants.

The Office has stated that the ARA used in Innis, et al. is from fungus origin (citing page 549), and the DHA is from fish oil origin (citing page 548). Applicants note, however, that the passage of Innis, et al. referred to by the Office as disclosing DHA from fish oil is actually describing a separate study that found that when fish oils containing DHA and eicosapentaenoic acid are included in formula without ARA,

[13] *See* Innis, et al. at abstract.

infant growth may be reduced.[14] In contrast to the Office's assertion, the Innis, et al. study described above used DHA from the alga *Crypthecodinium cohnii* and ARA from the fungus *Mortierella alpina*.[15] The Innis, et al. study thus used DHA and ARA from algal and fungal oil, not fish and fungal oil, as required by claim 1. Claim 1 is thus novel over Innis, et al.

The Office has also indicated that claiming a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.

As discussed above, whether or not a nutritional formula comprising DHA and ARA inherently results in an increase in lean body mass and a reduction in fat body mass when fed to a preterm infant **is irrelevant** to determining if Innis, et al. disclose applicants' claimed method. Claim 1 specifically requires a nutritional formula comprising DHA and ARA be administered to a preterm infant **for the purpose of** increasing lean body mass and reducing fat body mass in the infant. Thus, in order to anticipate applicants' claim 1, Innis, et al. must also disclose, either expressly or inherently, a method wherein a nutritional formula comprising DHA and ARA is administered to a preterm infant for the specific purpose of increasing lean body mass and reducing fat body mass in the infant. This is a limitation of applicants' claim 1 that cannot be ignored.

There is, however, clearly no disclosure or suggestion in Innis, et al. of administering a nutritional formula comprising

[14] *Id.* at p. 548, middle column.

DHA and ARA to a preterm infant for the purpose of increasing lean body mass and reducing fat body mass in the infant. At best Innis, et al. merely evaluate the effects of ARA and DHA supplemented formulas on the growth[16] or visual acuity of formula-fed premature infants. There is nothing in Innis, et al. that suggests that ARA and DHA have any affect on body composition, or more specifically, that ARA and DHA increase lean body mass and reduce fat body mass in infants.

Since Innis, et al. fail to disclose feeding a preterm infant a nutritional formula comprising DHA and ARA from fish and fungal oil for the purpose of increasing lean body mass and reducing fat body mass in the infant, Innis, et al. fail to disclose each and every limitation of claim 1. As such, claim 1 is novel over the cited reference.

Claim 5 depends from claim 1 and is thus patentable over the cited reference for the same reasons as set forth above for claim 1 as well as for the additional elements it requires.

New claim 23 is patentable over Innis, et al. for reasons similar to those set forth above for claim 1. Specifically, Innis, et al. fail to disclose feeding an infant a nutritional formula comprising a source of DHA and ARA for the purpose of increasing lean body mass and reducing fat body mass in the infant.

---

[15] *Id.* at p. 549 top of first column.
[16] Applicants note that Innis, et al. evaluate growth by measuring weight, length, and head circumference. *See* Innis, et al. at p. 549.

Additionally, with regard to new claim 24, applicants submit that Innis, et al. fail to disclose or suggest evaluating the lean body mass and fat body mass of an infant after feeding the infant a nutritional formula comprising DHA and ARA. Claim 24 is thus also patentable over Innis, et al.

4. Rejection of the Claims under 35 U.S.C. §103(a)

Reconsideration is requested of the rejection of claims 1-9 and 12-22 under 35 U.S.C. §103(a) as being unpatentable over O'Connor, et al. (U.S. Patent Application No. 2002/0045660) in view of Raclot, et al. ("Site-specific regulation of gene expression by n-3 polyunsaturated fatty acids in rat white adipose tissues," J. of Lipid Research, 1997, Vol. 38, p. 1963-1972).

O'Connor, et al. is discussed above. Significantly, O'Connor, et al. fail to disclose or suggest feeding a preterm infant a nutritional formula comprising DHA and ARA for the purpose of increasing lean body mass and reducing fat body mass in the infant. Raclot, et al. fail to overcome this deficiency.

Specifically, Raclot, et al. describe a study investigating whether fatty acid synthase (FAS), hormone-sensitive lipase (HSL), lipoprotein lipase (LPL), phosphoenolypyruvate carboxykinase (PEPCK), CCAAT/enhancer binding protein α (C/EBPα), and leptin mRNA levels are affected in retroperitoneal (RP) and subcutaneous adipose tissues (SC) of rats fed n-3 PUFAs. For four weeks, the rats were fed high fat diets (20% fat) containing n-3 PUFAs given as eicosapentaenoic acid (EPA

group), DHA, a mixture of EPA and DHA (MIX group), or native fish oil, or a control group fed with lard plus olive oil. Raclot, et al. found the fatty acid compositions of RP and SC to be similar and to resemble that of dietary fat within each experimental group. In RP, the FAS, HSL, PEPCK, LPL, C/EBPα, and leptin mRNA levels decreased as compared to control. In contrast, n-3 PUFAs had no affect on gene expression in SC. Raclot, et al. concluded that n-3 PUFAs (mainly DHA) affect gene expression in a site-dependent manner in white adipose tissues via possible antiadipogenic effects.

Significantly, however, Raclot, et al. fail to disclose or suggest feeding a preterm infant a nutritional formula comprising DHA and ARA for the purpose of increasing lean body mass and reducing fat body mass in the infant, as required by claim 1. Nor do Raclot, et al. disclose or suggest that nutritional formulas comprising the combination of ARA and DHA increase lean body mass and reduce fat body mass generally. Rather, as noted above, Raclot, et al. generally describe the effect of dietary n-3 PUFAs on adipose tissue gene expression in retroperitoneal and subcutaneous adipose tissues of rats. There is no disclosure in Raclot, et al. of how ARA, or more particularly the combination of ARA and DHA would affect adipose tissues of preterm infants, or more particularly lean muscle mass and fat body mass.

In order for the Office to show a *prima facie* case of obviousness, M.P.E.P. §2142 requires a clear articulation of the reasons why the claimed invention would have been obvious.

Specifically, the Supreme Court in KSR International Co. v. Teleflex Inc., 550 U.S. 398, 82 USPQ2d 1385, 1396 (2007) noted that the burden lies initially with the Office to provide an explicit analysis supporting a rejection under 35 U.S.C. 103. "[R]ejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some **articulated reasoning** with some **rational underpinning** to support the legal conclusion of obviousness."[17] The Court in *KSR International* further identified a number of rationales to support a conclusion of obviousness which are consistent with the proper "functional approach" to the determination of obviousness as laid down in Graham v. John Deere Co. (383 U.S. 1, 148 USPQ 459 (1966). Specifically, as previously required by the TSM (teaching, suggestion, motivation) approach to obviousness, one exemplary rationale indicated requires some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

Specifically, to reject a claim based on this rationale, the Office must articulate the following: (1) a finding that there was some teaching, suggestion, or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings to arrive at each and every limitation of the claimed invention; (2) a finding

[17] *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006) (emphasis added).

that there was reasonable expectation of success; and (3) whatever additional findings based on the *Graham* factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness. The Office has failed to meet its burden under number (1) above, as the cited references fail to show each and every limitation of Applicants' invention and there is no apparent reason for one skilled in the art to modify the references to arrive at each and every limitation. It simply would not have been obvious to one skilled in the art to arrive at Applicants' claimed combinations.

Initially, applicants note that none of the cited references disclose or suggest feeding a preterm infant a nutritional formula comprising DHA and ARA for the purpose of increasing lean body mass and reducing fat body mass in the infant, as required by claim 1. At best, O'Connor, et al. state that the ARA and DHA supplemented formulas described therein may improve or enhance neurological development, such as visual, motor, and language development, without findings of anthropometric growth faltering or inhibition. Nowhere, however, is there any suggestion that the formulas of O'Connor, et al. have any effect on body composition, such as increasing lean body mass and reducing fat body mass, or should be fed to a preterm infant for the specific purpose of increasing lean body mass and reducing fat body mass in the infant. The Raclot, et al. reference, while evaluating the effects of dietary n-3 PUFAs on gene expression in adipose tissue of rats, failed to suggest that the combination of DHA and ARA would increase lean muscle

mass and reduce fat body mass in preterm infants. Thus, the requirement in applicants' claim 1 that a nutritional formula comprising DHA and ARA be fed to a preterm infant for the specific purpose of increasing lean body mass and reducing fat body mass in the infant is entirely lacking from the cited references.

Nor is there apparent reason for one skilled in the art to modify the cited references to arrive at applicants' claimed method. As recognized by the Supreme Court in KSR International Co. v. Teleflex, Inc, while an obviousness determination is not a rigid formula, the TSM (teaching, suggestion, motivation) test captures a helpful insight: "A patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs [caution as to] a patent application that claims as innovation the combination of two known [elements] according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the [art] to combine the elements in the way the claimed new invention does."[18]

As discussed in the specification of the instant application, applicants' have discovered that infants fed a nutritional formula comprising DHA and ARA, or a suitable source thereof, can increase lean body mass and reduce fat body mass as compared to an unsupplemented control formula, without having an

[18] 2007 WL at 5.

impact on the rate of overall growth of the infant.[19] In contrast, none of the cited references disclose or recognize that the combination of DHA and ARA has any effect on body mass, or more specifically can result in an increase lean body mass and a reduction in fat body mass in infants. Given this lack of disclosure and recognition, why would one skilled in the art modify the teachings of the cited reference to arrive at a method comprising feeding a preterm infant a nutritional formula comprising DHA and ARA for the specific purpose of increasing lean body mass and reducing fat body mass in the infant, as required in the method of Applicants' claim 1? There is simply no apparent reason to make this modification.

Accordingly, there is no articulated reason to combine or modify the teachings of the cited references to arrive at each and every limitation of Applicants' claim 1. As such, claim 1 cannot be said to be obvious in view of the cited references.

In the current action, the Office has stated that it would have been obvious to include ARA and DHA in a preterm infant formula to achieve an increase in the muscular tissue while limiting the increase in fat cell size as disclosed by the combination of O'Connor, et al. and Raclot, et al. Applicants respectfully disagree.

For the reasons set forth above, neither of the cited references, alone or in combination, suggest that the combination of ARA and DHA, when fed to a preterm infant, could

[19] *See* Specification at p. 2, lines 13-16, and 24-27.

increase the lean body mass and reduce the fat body mass of the infant. Although Raclot, et al. do state that dietary n-3 PUFAs limit abdominal fat deposit hypertrophy, Raclot, et al. says nothing about the effect the combination of DHA and ARA would have on abdominal fat deposit hypertrophy. As will be recognized by those skilled in the art, changing the combination of polyunsaturated fatty acids present in an infant formula can alter how the formula affects the infant, be it in changes in growth, neurological development, etc. In the instant case, there is nothing in either of the cited references to suggest that the specific combination of DHA and ARA would result in an increase in lean body mass and a reduction in fat body mass when administered to a preterm infant in a nutritional formula.

Applicants again note that claim 1 specifically requires a nutritional formula comprising DHA and ARA be administered to an infant for the purpose of increasing lean body mass and reducing fat body mass in the infant. This limitation is not met merely by the disclosure of feeding a nutritional formula comprising ARA and DHA to an infant. Rather, there must be some disclosure in the cited references of a method wherein a nutritional formula comprising DHA and ARA is administered to a preterm infant for the specific purpose of increasing lean body mass and reducing fat body mass in the infant. Whether or not a nutritional formula comprising DHA and ARA inherently results in an increase in lean body mass and a reduction in fat body mass when fed to an infant is irrelevant to determining if the cited references disclose or suggest applicants' claimed method. In the instant case, none of the cited references disclose or

suggest that the combination of DHA and ARA has any effect whatsoever on lean body mass and fat body mass, much less suggest feeding a preterm infant a nutritional formula comprising DHA and ARA for the specific purpose of increasing lean body mass and reducing fat body mass in the infant.

As claims 2-9 and 12-16 depend directly or indirectly from claim 1, claims 2-9 and 12-16 are patentable for the same reasons as claim 1, as well as for the additional elements they require.

Furthermore, with regard to claim 17, applicants note that none of the cited references disclose evaluating the lean body mass and fat body mass of an infant after feeding the infant a nutritional formula comprising DHA and ARA. Claim 17 is thus also patentable over the cited references.

Claims 18-19 depend from claim 17 and are thus patentable over the cited reference for the same reasons as set forth above for claim 17, as well as for the additional elements they require.

Independent claims 20 and 22 and new claim 23 are patentable over the cited references for the same reasons as set forth above for claim 1.

Claim 21 depends from claim 20 and thus is patentable over the cited references for the same reasons as set forth above for claim 20, as well as for the additional elements it requires.

New claim 24 is patentable over the cited references for the same reasons as set forth above for claim 17.

CONCLUSION

In light of the foregoing, applicants request withdrawal of the rejections of claims 1-9 and 12-22 and allowance of all pending claims. The Commissioner is hereby authorized to charge any government fees which may be required to Deposit Account No. 01-0025.

Respectfully Submitted,

/Christopher M. Goff/

Christopher M. Goff, Reg. No. 41,785
ARMSTRONG TEASDALE LLP
One Metropolitan Square, 26th Floor
St. Louis, Missouri 63102
314-621-5070

CMG/LJH/ts
By EFS